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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/229,173      | 01/13/1999  | DEB K. CHATTERJEE    | 0942.2800008        | 7438             |

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EXAMINER  
HUTSON, RICHARD G

ART UNIT                    PAPER NUMBER  
1652                    22

DATE MAILED: 01/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

|                        |                               |                                    |
|------------------------|-------------------------------|------------------------------------|
| <b>Advisory Action</b> | Application No.<br>09/229,173 | Applicant(s)<br>CHATTERJEE, DEB K. |
|                        | Examiner<br>Richard G Hutson  | Art Unit<br>1652                   |

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 18 December 2001 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a)  The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.
- b)  The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.  
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.  A Notice of Appeal was filed on 18 December 2001. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.  The proposed amendment(s) will not be entered because:

- (a)  they raise new issues that would require further consideration and/or search (see NOTE below);
- (b)  they raise the issue of new matter (see Note below);
- (c)  they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d)  they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_.

3.  Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.

4.  Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.  The a) affidavit, b) exhibit, or c) request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.

6.  The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.  For purposes of Appeal, the proposed amendment(s) a) will not be entered or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 1,3-10,13,16,17,19,26,28,29 and 34-44.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

8.  The proposed drawing correction filed on \_\_\_\_\_ is a) approved or b) disapproved by the Examiner.

9.  Note the attached Information Disclosure Statement(s) ( PTO-1449) Paper No(s). \_\_\_\_\_.

10.  Other: \_\_\_\_\_

Continuation of 5. does NOT place the application in condition for allowance because: Claims 1, 3-10, 13, 16, 17, 19, 26, 28, 29 and 34-44 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is stated in the previous office action.

Applicants disagree with this rejection and submit that one of skill in the art could reasonably conclude that applicants had possession of the Tma DNA polymerase mutants encompassed by the rejected claims in the present application as filed. Applicants submit that the Examiner has underestimated both the teaching of the present application and the level of skill in the art and the examiner has done nothing more than argue lack of literal support in the application, failing to present evidence or reasons why one skilled in the art would not reasonably conclude that applicants were in possession of the subject matter of the rejected claims. Applicants submit that the standard for fulfilling the written description requirement is whether the specification provides sufficient disclosure for one skilled in the art to readily envision a representative number of members of the claimed genus. Applicants further submit that at the time the invention was made, the sequence of many DNA polymerases had been compiled and aligned, showing that the DNA polymerases could be divided into several distinct families based on sequence homology. These distinct families of polymerases share many conserved sites throughout the protein and domains responsible for the various activities of the polymerases have been identified. Further still it has been shown that a number of mutations in the different polymerases within a family appear to be conserved throughout the family such that they result in the same functional modification of many of the polymerases of that family. Based on this information available at the time of filing, applicants assert that one skilled in the art could readily envision a representative number of members of the claimed genus. Applicant is reminded that the rejected claims are not rejected based on a lack of enablement, but rather a lack of adequate written description. The claimed genus includes all possible *Thermotoga maritima* (Tma) DNA polymerase mutants which are modified at least two ways selected from the group consisting of (a) to reduce or eliminate the 3' 5' exonuclease activity of the polymerase; (b) to reduce or eliminate the 5' 3' exonuclease activity of the polymerase; and (c) to reduce or eliminate discriminatory behavior against a dideoxynucleotides and methods of using and kits comprising said DNA polymerase mutants and genes encoding said DNA polymerase mutants. As stated in the previous office action, there is no disclosure of any particular structure to function/activity relationship in the claimed genus. While the specification provides the species, Asp323 -Ala323, (having reduced 3' -5' exonuclease activity), Phe730 -Tyr730 (having reduced discriminatory behavior against a dideoxynucleotides) and Asp8 -Ala8, Asp137 -Ala137 or the deletion of 219 amino terminal amino acids of Tma DNA Polymerase (having reduced 5' 3' exonuclease activity) encompassed by these claims, the specification clearly does not disclose a representative number of species of the claimed genus which includes an infinite number of amino acid variants as well as additional chemical modifications of any Tma DNA polymerases. Even considering the substantial knowledge of the skilled artisan, as detailed by applicants, one could only envision a small number of additional species within the scope of the claimed genus. However, in view of the enormous breadth of the claimed genus, even these could in no way be considered to be representative of the entire genus. There is no disclosure of any particular structure to function/activity relationship in the claimed genus. The claimed genus of mutant Tma DNA polymerases has no structural limitation, only a functional limitation, thus the infinite number of species encompassed by this genus has not been adequately described by the few species disclosed in the specification.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at [www.uspto.gov](http://www.uspto.gov).



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